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REMARKS

This is response to the non-Final Office action (Paper No. 20061110) mailed 14 November 2006.

Claims 1, 5-9, 21 and 22 are pending in this application.

Claims 1 and 22 have been amended, and claims 23 and 24 have been newly added.

No new matter has been added.

I. Claim Rejections – 35 USC §102

1. Claims 1, 7 and 21 stand rejected under 35 U.S.C. 102(b) as being anticipated by Keller *et al.* ("Molecular evolution of the CMT1A-REP region: a human- and chimpanzee-specific repeat. Mol Biol Evol. 1999 Aug; 16(8): 1019-26").

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

(1) Claim 1

The examiner failed to show that each and every element as set forth in the claim 1 is found in Keller et al.

(a) "said Alu element being more enriched in the human genome than in any non-human primate genome"

Since claim 1 has been amended to another equivalent term, there is no change of the scopes of the claims, and there is no surrender of any scope of the claims.

Please note that, when a countable noun is used in a plural form, it is a generic noun (*i.e.*, representative of all members of a group). The "non-human primate genomes" is a generic noun. The examiner unreasonably interpreted "non-human primate genomes" as "some non-human primate genomes".

The examiner argued that the feature of "said Alu element being enriched in the human genome compared to non-human primates genomes" is found in Keller et al. in page 1023, Fig. 3c, lane hu, for example. The examiner argued that Fig. 3c of Keller et al. shows that the amplification was observed in the human and two chimpanzee species, and not observed in, for example, gorilla and galago, and that thus, the Alu element in Keller et al. is enriched in the human genome compared to non-human primates genomes.

The examiner's interpretation is not reasonable and is not consistent with the interpretation that those skilled in the art would reach. During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (emphasis added). The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999). See MPEP 2111.

In view of the broadest reasonable interpretation consistent with the specification, and/or consistent with the interpretation that those skilled in the art would reach (*In re Cortright*, 165

F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999), see MPEP 2111), the reasonable person would reach that the "compared to the non-human primates genomes" does not mean "compared to a few specific non-human primates genomes." Also, recently the court held that the PTO should apply the principles of *Phillips v. AWH* during prosecution. ("It is well established that dictionary definitions must give way to the meaning imparted by the specification, *Phillips v. AWH Industries*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*)" *In re Johnston*, Case No. 05-1321 (Fed. Cir. 2006).

Here, it cannot be determined that the Alu element of Keller et al. is more enriched in the human genome than in any non-human primate genome. Fig. 3c of Keller et al. does not show whether the Alu element is more enriched in the human genome than, for example, two chimpanzee species. Keller et al. did not show that there is a higher copy number of the Alu repeats in the human genome than in any non-human primate genome. Regarding this argument, the examiner also argued that this argument is not commensurate in scope with the claimed invention, and the claimed invention does not require the detection of determination of, "copy number" of the Alu sequences. The feature of "said Alu element being more enriched in the human genome than in any non-human primate genome" necessarily means that there is a higher copy number of said Alu element in the human genome than in any non-human primate genome. The applicant respectfully asked the examiner to explain how the Alu element is more enriched in the human genome than in any non-human primate genomes, without considering the copy number of the Alu element.

Since each and every element is not found in Keller et al., claims 1 and 7 are not anticipated by Keller et al.

(b) "the amplification being intra-Alu polymerase chain reaction amplification"

The examiner argued that the intra-Alu PCR is disclosed in Fig. 1, primers P1/C1, P2/T1, D1/C1, T1/D2; pages 1020, 1021, materials and methods, polymerase chain reaction, for example.

However, intra-Alu PCR is not shown in Keller et al. As shown in Sifis et al., and the present invention, intra-Alu PCR generates a homogenous product composed entirely of repeat core-unit DNA sequences characteristic of the element being amplified. The PCR in Keller et al. amplifies the centromeric boundary of the proximal REP even if the amplicon includes an Alu element. That is, the PCR in Keller et al. does not generate a product composed entirely of repeat Alu-element sequences. If the examiner disagrees with the applicant's argument, please provide what the examiner's definition of the intra-Alu PCR is.

Since each and every element is not found in Keller et al., claims 1 and 7 are not anticipated by Keller et al.

(c) "measuring the amount of the human DNA by comparing the amplified DNA with a reference"

The examiner repeatedly argued that merely comparison of the bands in an ethidium stained gel is encompassed by "quantitating the human DNA by comparing the amplified DNA with a reference." While the comparison of the band of the amplified human DNA to another band with a known amount of the human DNA may tell which has more human DNA quantity, merely comparing the human DNA band to the non-human primate DNA band does tell neither the quantity of the human DNA nor the a greater or lesser quantity of DNA than another because the human genome and the non-human genome have different copy numbers of the Alu repeats.

In other words, even if the band of the amplified human DNA is stronger than the band of the amplified non-human primate DNA, it does not necessarily mean that the quantity of the human DNA is greater than the quantity of the non-human primate DNA unless the human DNA and the non-human primate DNA have the same copy number of the Alu repeats. The applicant showed why the quantitation of the human DNA cannot be achieved by merely comparison of the bands in an ethidium stained gel with another non-human primate genomes. In order to be qualified as prior art is that the reference must enable an ordinary skilled person to practice the invention as claimed. The applicant showed why the examiner's argument is not proper because the Keller et al. does not enable an ordinary skilled person to measure the amount of the human DNA, even the relative amount of the human DNA compared to the non-human primate DNA.

In addition, assuming that a person gets the band which looks like the first three lanes (*i.e.*, "hu", "pc" or "cc") in Fig. 3c from the polymerase chain reaction of an unknown sample, how can the person know whether the band is of the human DNA or of the common chimpanzee or the mixture of the human DNA and the common chimpanzee DNA? Fig. 3c does not show even the relative quantity, but merely shows the existence of a specific band.

In response to the applicant's arguments for showing that the prior art is not enabling, the examiner did not provide any explanation in response to the above argument, and did merely conclude that measurement of the amount of the human DNA is clearly encompassed by the visual comparison with a band for another non-human primate. ("In order to provide a complete application file history and to enhance the clarity of the prosecution history record, an examiner must provide clear explanations of all actions taken by the examiner during prosecution of an application", and "Where the applicant traverses any rejection, the examiner should, if he or she

repeats the rejection, take note of the applicant's argument and answer the substance of it." See MPEP §707.07(f).)

Also, the examiner unreasonably argued that claim 1 recites "measurement by comparison". Claim 1 recites "measuring **the amount** of the human DNA by comparing the amplified DNA with a reference" (emphasis added). The examiner repeatedly did not consider the feature of "the amount" and did unreasonably argue that the copy number of the Alu sequences is not relevant to the present invention.

Withdrawal of the rejection is respectfully requested.

(2) Claim 7

Claim 7 depends from claim 1. Since claim 1 is patentable, claim 7 is also patentable.

(3) Claim 21

The examiner failed to show that each and every element as set forth in the claim 21 is found in Keller et al.

(a) "said *Alu* element being present only in the human genome"

The examiner argued that the feature of the Alu element is present only within the human genome is found in Keller et al. because it discloses comparison between lane hu and lanes go-ga, for example, and it is claimed in "comprising" language, which allows for the incorporation of additional method steps.

The examiner's interpretation is unreasonable.

The term "only" means "without anyone or anything else; alone". (The American Heritage Dictionary of the English Language, Third Edition, Houghton Mifflin Company) It is

hardly understood what the examiner's definition of the term "only". The examiner's interpretation of the above feature is that said *Alu* element is present only in the human genome, is not present in a certain non-human genome, and may be present in some non-human genome.

The examiner argument of that "it is claimed in "comprising" language, which allows for the incorporation of additional method steps" is hardly understood. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The examiner must show the feature of "said *Alu* element being present only in the human genome" in Keller et al. regardless of the kinds of the transitional term. The transitional term "comprising" cannot be used to change the expressly recited feature of ""said *Alu* element being present only in the human genome" into "said *Alu* element is present only in the human genome, is not present in a certain non-human genome, and may be present in some non-human genome."

Since the examiner did not show all the features recited in claim 21, claim 21 is not anticipated by Keller et al.

(b) "the amplification being intra-Alu polymerase chain reaction amplification"

The applicants showed why this limitation is not found in Keller et al. in traversing the examiner's rejection of claim 1.

Since each and every element is not found in Keller et al., claims 1 and 7 are not anticipated by Keller et al.

(c) "measuring the amount of the human DNA by comparing the amplified DNA with a reference"

The applicants showed why this limitation is not found in Keller et al. in traversing the examiner's rejection of claim 1.

Since each and every element is not found in Keller et al., claims 1 and 7 are not anticipated by Keller et al.

Withdrawal of the rejection is respectfully requested.

II. Claim Rejections – 35 USC §103

1. Claims 1, 7, 8 and 22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis *et al.* ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May; 47(3): 589-92) in view of Palmirotta *et al.* ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143 - §2143.03 for decisions pertinent to each of these criteria.

The examiner failed to establish the *prima facie* case of obviousness because the above three basic criteria are not met.

(1) The prior art references when combined do not teach or suggest all the claim limitations.

Claim 1 recites "said Alu element being more enriched in the human genome than in any non-human primate genome", and claim 22 recites "a copy number of said predetermined genomic DNA in the human genome being higher than a copy number of said predetermined genomic DNA in any non-human primate genome".

The examiner admitted that these features are not found in Sifis et al., and acknowledged that an Alu sequence in Palmirotta et al. that occurs in humans as well as non-human primates can lead to inconclusive results. That is, the examiner did not show that "said Alu element being more enriched in the human genome than in any non-human primate genome" is found in the prior art.

To make up for this deficiency, the examiner argued that from these disadvantages of the prior art, "it was routine practice to one of skill in the art at the time of invention to incorporate controls within experiments to test for correct function of the procedure or process."

The examiner's burden is to show how the ordinary skilled person can correct the problems of the prior art references. Merely showing that there is a general incentive is not enough. ("The general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out." *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).) While a "general incentive" may make an approach "obvious to try" it does not make the invention obvious. "Obvious to try" is not the standard of

obviousness under 35 U.S.C. §103. In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988).

As in *In re Deuel*[1], the examiner merely showed that there is a general incentive. Thus, Sifis et al.'s teachings, even in combination with Palmirotta, fail to suggest the claimed invention.

Since the examiner admitted that the prior art references do not show all the features recited in claims 1 and 22, and merely showed a general incentive, the examiner failed to establish a prima facie case of obviousness.

Additionally, the following points must be considered when determining obviousness. MPEP §2141.35 states that "[s]uch secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquires may have relevancy."

Here, as admitted by the examiner, Palmirotta et al. and Sifis et al. failed to show the specificity of their intra-Alu amplification. Sifis et al. acknowledged that forensic samples are often contaminated with nonhuman DNA, and they make no attempt to determine the specificity of their intra-Alu amplification, and, in Palmirotta et al., it cannot be determined whether the statue blood originated from humans or from a non-human catarrhine primate. If, as stated by the examiner, this problem is obvious and the solution for the problem is obvious, why do

[1] In *In re Deuel*, the court stated that "even if, as the examiner stated, the existence of general cloning techniques, coupled with knowledge of a protein's structure, might have provided motivation to prepare a cDNA or made it obvious to prepare a cDNA, that does not necessarily make obvious a particular claimed cDNA. "Obvious to try" has long been held not to constitute obviousness. *In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988).* A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. Thus, Maniatis's teachings, even in combination with Bohlen, fail to suggest the claimed invention." ." *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).

Palmirotta et al. and Sifis et al. use non-specific methods? Long felt but unsolved needs and failure of Sifis et al. and Palmirotta et al., assist in establishing the nonobviousness of an applicant's invention.

For the foregoing reasons, claims 1 and 22 and its dependent claims 7 and 8 are not obvious over Sifis *et al.* in view of Palmirotta *et al.*

2. Claims 5 and 22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis *et al.* ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May; 47(3): 589-92) in view of Palmirotta *et al.* ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252), Buck *et al.* ("Design Strategies and Performance of Custom DNA Sequencing Primers" BioTechniques. September 1999. 27: Pages 528-536).

The examiner admitted that SEQ ID NOs:3 and 4 are not taught in Sifis et al. and Palmirotta et al, but are contained in Jurka. The examiner cited *In re Deuel* for a prima facie case of obviousness based on a structural similarity, and argued that the claimed primers simply represent complementary functional homologs of the sequences taught by Jurka.

(1) First, the recited primer sequences are not suggested by the prior art references, and a general motivation to search the primer is not sufficient to establish a prima facie case of obviousness.

In *In re Deuel*, the court held that "[t]he PTO's theory that one might have been motivated to try to do what Deuel in fact accomplished amounts to speculation and an

impermissible hindsight reconstruction of the claimed invention. It also ignores the fact that claims 5 and 7 are limited to specific compounds, and **any motivation that existed was a general one, to try to obtain a gene that was yet undefined and may have constituted many forms**. A general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search. More is needed and it is not found here." *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995) (emphasis added.).

U.S. PTO and the Courts have recognized that the DNA fragment is an isolated compound that is different from the full length gene compound. Because the DNA fragment and the full-length gene are different compounds, the full-length gene sequence forming part of the state of the art is not novelty destroying to the DNA fragment.

Here, likewise, a prior art disclosing the sequence of a certain gene does not automatically make the particular DNA primers amplifying the specific region of the certain gene obvious. Also, vast number of the primers could be deduced from the known protein sequence. Obvious to try has long been held not to constitute obviousness. The examiner merely showed the full length gene compound and argued a general motivation to search for primers. As stated in *In re Deuel*, the general motivation to search does not necessarily make obvious a specifically-defined gene.

Since the prior art references do not suggest the recited primer sequences, the prior art references are lacking here with respect to the recited primers.

For the foregoing reasons, the examiner failed to establish a prima facie case of obviousness.

Second, the examiner's reasoning based on Buck is not proper.

With respect to the issue of reasonable expectation of success, the examiner improperly cited Buck. Please note that Buck compares the primers for the exact same 300-bp sequence *in automated DNA sequencing*, using the same PCR reaction condition. If the targets are different and/or the PCR reactions are different, and/or the purposes are different, the PCR primers will not yield the data of the same quality.

The examiner misunderstood Buck's teaching. Buck's teaching can be applied only to the case where the primers are for the exact same sequence in automated DNA sequencing.

For example, unlike Buck'teaching, different primers for the purpose of quantitation of human DNA result in different detection limits and different specificities, and, when there are primate DNA other than human DNA in a sample, different primers may result in different artifact Amplicons from DNA of other species as a result of sequence similarity to SINE elements from other species. Since the purpose of Buck et al. was automated DNA sequencing, these factors were not considered. It should be also noted that the design of a PCR assay may involve tradeoffs among competing objectives, and extensive analysis is required. The result for automated DNA sequencing cannot be applied to the human DNA quantitation method.

The examiner unreasonably applied the Buck's teaching to the quantitation of human DNA.

For the foregoing reasons, there is no reasonable expectation of success.

Please note that, with respect to claim 22, the examiner rejected claim 22 on the basis of Sifis et al. in view of Palmirotta et al., and also rejected claim 22 on the basis of Sifis et al. in view of Palmirotta et al., in further in view of Jurka and Buck et al. without reasoning. Please clarify what the examiner's reasoning of the rejection of claim 22 on the basis of Sifis et al. in

view of Palmirotta et al., in further in view of Jurka and Buck et al. is. (Is it different from the rejection based on Sifis et al. in view of Palmirotta et al.?)

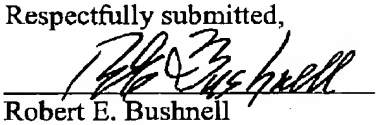
3. Claim 9 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis *et al.* in view of Palmirotta *et al.*, in further view of Gelmini *et al.*, over Keller *et al.* in view of Gelmini *et al.*

Claim 9 depends from claim 1. Since claim 1 is patentable, claim 9 is also patentable.

No fees are incurred by this Amendment.

In view of the above, all claims are submitted to be allowable and this application is believed to be in condition to be passed to issue. Reconsideration of the rejections is requested. Should any questions remain unresolved, the Examiner is requested to telephone Applicant's attorney.

Respectfully submitted,



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